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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/621,268	07/21/2000	STEPHEN D. GILLES	LEX-007	3473
21323	7590	04/13/2004	EXAMINER	
TESTA, HURWITZ & THIBEAULT, LLP HIGH STREET TOWER 125 HIGH STREET BOSTON, MA 02110			CANELLA, KAREN A	
			ART UNIT	PAPER NUMBER
			1642	

DATE MAILED: 04/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/621,268	GILLES ET AL.	
	Examiner	Art Unit	
	Karen A Canella	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on ____.
 2a) This action is FINAL. 2b) This action is non-final.
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-9, 11-16, 18-21, 24-26 and 47 is/are pending in the application.
 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
 5) Claim(s) _____ is/are allowed.
 6) Claim(s) 1-9, 11-16, 18-21, 24-26 and 47 is/are rejected.
 7) Claim(s) _____ is/are objected to.
 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ . |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>20031124 + 2003092</u> . | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| | 6) <input type="checkbox"/> Other: _____ . |

DETAILED ACTION

Please note that the amendment filed January 7, 2004 is not labeled with the correct serial number. In future correspondence please check papers before filing for the correct serial number because the incorrect serial number can result in entry delay, or entry into another case.

Claims 1, 8, 9, 12, 15, 16, 24 and 26 have been amended. Claims 10, 17, 22, 23 and 27-46 have been canceled. Claim 47 has been added. Claims 1-9, 11-16, 18-21, 24-26 and 47 are pending and under consideration.

Claims 1-3, 5, 6, 7, 14, 15, 18-20, 24 and 25 are rejected under 103(a) as being unpatentable over Falkenberg et al (US 6,406,689, cited in the previous Office action) in view of Steinman et al (WO 93/20185) and Sallusto et al (Journal of Experimental Medicine, 1994, vol. 179, pp. 1109-1118) and de La Salle et al ('Fcgr on Human Dendritic Cells' In:Human IgG Receptors, 1996, pp. 39-55, Van de Winkel et al Eds).

Claim 1 is drawn to a method for enhancing the immunogenicity of an antigen in a mammal the method comprising administering intramuscularly, intravenously, transdermally or subcutaneously, a fusion protein comprising an antigen linked by a polypeptide bond to an immunoglobulin heavy chain constant region whose ability to bind an Fc receptor is not modified by mutation thereby to elicit an immune response against the antigen, wherein the fusion protein lacks an immunoglobulin variable domain and the antigen is selected from the group consisting of PSMA, an ectodoamin of a cytokine receptor, a viral protein and a tumor-specific protein, the antigen of the fusion protein eliciting a stronger immune response in the mammal than the antigen alone. Claim 2 embodies the method of claim 1 further comprising administering the fusion protein in combination with an adjuvant in an amount sufficient to enhance the immune response against the antigen of the fusion protein relative to the immune response against the antigen of the fusion protein administered without the adjuvant. Claim 3 embodies the method of claim 2 wherein the fusion protein and adjuvant are administered simultaneously. Claim 5 embodies the method of claim 1 wherein the immunoglobulin heavy chain constant region comprises an immunoglobulin hinge region. claim 6 embodies the method of claim 5 wherein the immunoglobulin heavy chain constant region comprises an

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immunoglobulin heavy chain constant region domain selected from the group consisting of a CH2 domain, a CH3 domain and a CH4 domain. Claim 7 embodies the method of claim 5 wherein the immunoglobulin heavy chain constant region comprises a CH2 domain and a CH3 domain. Claim 14 comprises the method of claim 1 wherein the mammal is a human.

Claim 15 is drawn to a composition for eliciting an immune response against an antigen in a mammal, the composition comprising an adjuvant and antigen fusion protein comprising an antigen linked by a polypeptide bond to an immunoglobulin heavy chain constant region whose ability to bind an Fc receptor is not modified by mutation thereby to elicit an immune response against the antigen, wherein the fusion protein lacks an immunoglobulin variable domain and the antigen is selected from the group consisting of PSMA, an ectodoamin of a cytokine receptor, a viral protein and a tumor-specific protein, the composition being formulated for intramuscular, intravenous, transdermal or subcutaneous administration. Claim 18 embodies the composition of claim 15 wherein the immunoglobulin heavy chain constant region comprises an immunoglobulin hinge region. Claim 19 embodies the composition of claim 18 wherein the immunoglobulin heavy chain constant region comprises a domain selected from the group consisting of a CH2 domain, a CH3 domain, and a CH4 domain. Claim 20 embodies the composition of claim 18 wherein the immunoglobulin heavy chain constant region comprises a CH2 domain and a CH3 domain. Claim 24 embodies the composition of claim 15 wherein the adjuvant comprises a cytokine. Claim 25 comprises the composition of claim 24 wherein the cytokine is a human cytokine.

Falkenberg et al teach a method of enhancing the immunogenicity of an antigen in a mammal comprising administering to said mammal intramuscularly, or subcutaneously a dose of inactivated tumor cells or tumor cell portions (column 20, under the heading of "The tumor Cells and tumor Cell Portions") and a dose of recombinant IL-2 as adjuvant (column 21, under the heading of "Immunostimulants" and column 22, lines 49-53, column 17, lines 16-19 and column 5, lines 38-40). Falkenberg et al teach that adjuvants can be administered prior to, simultaneous with or following the administration of an antigen (column 3, lines 4-45). Falkenberg et al teach recombinant human IL-2 as the preferred embodiment of adjuvant (column 17, lines 16-19). Falkenberg et al do not teach the fusion of a tumor associated antigen with the immunoglobulin Fc domain or portion thereof.

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Steinman et al teach that dendritic cells are termed "nature's adjuvant" because aid cells are capable of directly priming T cells that recognize only antigens presented by the particular MHC class of the presenting dendritic cell and because dendritic cells are capable of capturing antigens in an immunogenic form in situ (page 33, lines 16-23). Steinman et al include tumor antigens as the antigens presented by dendritic cells (page 33, lines 14-16). Steinman et al teach that dendritic cells are capable of processing complex antigens into those peptides that would be presented by self MHC products (page 33, lines 29-31).

Sallusto et al teach that the efficiency of soluble antigen presentation by dendritic cells can be enhanced by specific antibodies via Fc Receptor-mediated antigen uptake (title and abstract, lines 8-10). Sallusto et al teach that dendritic cells have pinocytic activity and that the Fc receptor II on dendritic cells can be used to increase the uptake of antigen in antigen-antibody complexes (page 1110, first column, lines 11-13) which results in antigen-presentation and stimulation of naive T-cells (page 1110, first column, lines 5-6 and lines 13-16). Sallusto et al teach that dendritic cells were the most effective of the antigen-presenting cells at presenting a soluble antigen and that in the presence of the antibody that binds to said antigen presentation increased 100-fold (page 1111-1112, under the heading "Efficient presentation of soluble Antigen and Antibody-antigen complexes by Immature Dendritic Cells" and page 1115, second column, lines 16-20).

De la Salle et al teach that presentation of exogenous soluble antigens to helper T-cells is a complex process which requires uptake of proteins by antigen presenting cells, digestion of said proteins into immunogenic peptides, the intracellular association of the immunogenic peptides with MHC II molecules and the transport of the resulting immunogenic complexes to the plasma membrane for recognition by antigen specific T-cells (page 46, lines 20-26). De la Salle et al teach that targeting of antigens to Fcgamm Receptor on Langerhans cells by means of immune complexes comprising IgG complexed to its target soluble antigen resulted in antigen presentation at dramatically reduced levels of soluble antigen and that this process required both the uptake of immune complexes via the Fcgamma receptor and the processing of the antibody-complexed soluble antigen by the Langerhan's cells (page 46, lines 37-45).

It would have been *prima facie* obvious at the time the invention was made to replace the administration of "tumor cell portions" with tumor cell antigens fused to the Fc region of the

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immunoglobulin heavy chain domain in order to target the tumor antigen to the Fc receptor of dendritic cells. One of skill in the art would have been motivated to do so because of the teachings of Steinman et al regarding the presentation of tumor cell antigens by dendritic cells; and the teachings of Sallusto et al and De la Salle regarding the increased efficiency of antigen presentation on dendritic cell through the Fcgamma receptor on dendritic cells. One of skill in the art would conclude that although Sallusto et al and de la Salle et al documented this increased efficiency of soluble antigen presentation using antigen-antibody immune complexes, the target was the dendritic cell Fc gamma receptor which bound the antibody-antigen complex via the Fc domain of the antibody, and therefore it flows logically from this that a fusion protein comprising the Fc domain of the antibody and an antigen would also bind to the Fcgamm receptor of the dendritic cells. thus, one of skill in the art would expect that said fusion protein would be internalized and the antigen processed and presented on the surface of the dendritic cell in the same manner and as immune complex which was internalized via the dendritic cell Fcgamm receptor. It would be obvious that the resulting method would cause a greater presentation of tumor antigen to T-cells of the host and thus would result in a stronger immune response in the mammal than the antigen alone.

Claims 1-3, 5, 6, 7, 14, 15, 18-20, 24 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over as applied to claim above, and further in view of Hurn and Chantler ('Production of Reagent Antibodies' In: Methods in Enzymology, 1980, Vol. 70, pp. 189-193).

Claims 1 and 15 contain the specific embodiments of intramuscular, intravenous, transdermal or subcutaneous administration. Falkenberg et al teach intramuscular or subcutaneous administration. Frankenberg et al do not specifically teach intravenous or transdermal administration.

Hurn and Chantler teach the introduction of soluble immunogen at intravenous, intramuscular, subcutaneous, intraperitoneal, intradermal, intraarticular or intranodal sites (page 112, lines 12-23).
KA L
4/8/04

It would have been prima facie obvious at the time the invention was made to introduce the fusion protein rendered obvious by the combination of Falkenberg et al and Steinman et al and Sallusto et al and de la Salle et al by subcutaneous and intravenous routes of administration.

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One of skill in the art would be motivated to do so by the teachings of Hurn and Chantler that the intravenous administration is more efficient at provoking an immune response than intramuscular injection; and further one of skill in the art would know that for the treatment of human patients, subcutaneous administration, although not as effective in inducing an immune response, would be easier than intravenous administration, as it does not require venipuncture techniques.

Claims 1-7, 11-16, 18-20, 24, 25 and 47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Falkenberg et al and Steinman et al and Sallusto et al and De La Salle et al as applied to claims 1-3, 5, 6, 7, 14, 15, 18-20, 24 and 25 above, and further in view of Ward (US 6,277,375, cited in the previous Office action).

Claim 4 embodies the method of claim 2 wherein the adjuvant comprises a fusion protein comprising an immunoglobulin heavy chain constant region linked by a polypeptide bound to an adjuvant protein. Claim 11 embodies the method of claim 4 wherein the adjuvant protein is a cytokine. Claim 12 embodies the method of claim 11 wherein the cytokine is a cytokine present in the same species of the mammal. Claim 13 embodies the method of claim 12 wherein the cytokine is a human cytokine. Claim 16 embodies the composition of claim 15 wherein the adjuvant comprises a fusion protein comprising an immunoglobulin constant region linked by a polypeptide bond to an adjuvant protein.

The combination of Falkenberg et al and Steinman et al and Sallusto et al and de la Salle et al renders obvious the method and composition wherein the adjuvant is IL-2 for the reason set forth above. none of the aforesaid references teach or suggest a method wherein the adjuvant comprises a fusion protein comprising an immunoglobulin constant region linked by a polypeptide bond to an adjuvant protein. It is noted that the limitation of "whose ability to bind an Fc receptor is not modified by mutation" has not been applied to the adjuvant fusion protein.

Ward teaches recombinant vector encoding IL-2 linked to a mutant Fc hinge or mutant Fc domain (column 7, lines 22-35). Ward et al teach that the mutant Fc hinge region results in increased serum half-life (column 7, lines 22-34).

It would have been prima facie obvious at the time the invention was made to administer the IL-2 in the method rendered obvious by the combination of Falkenberg et al and Steinman et

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al and Sallusto et al and de la Salle et al as IL-2 fused to a mutant immunoglobulin hinge region or mutant immunoglobulin constant domain. One of skill in the art would have been motivated to do so by the teachings of Ward et al regarding the increase in serum half life expected for IL-2 fused to a mutant Fc or mutant Fc hinge. One of skill in the art would be motivated to increase the serum half life of the IL-2 in order to prolong the time which the administered IL-2 can exert its adjuvant properties on immune effector cells. further, one of skill in the art would be motivated to linked the IL-2 to a mutant Fc hinge or mutant Fc constant region in order to avoid uptake and processing of said IL-2 by antigen presenting cells and subsequent immune reaction against the administered IL-2.

Claims 1-3, 5-9, 14, 15, 18-20, 24 and 25 are rejected under 103(a) as being unpatentable over Falkenberg et al (US 6,406,689, cited in the previous Office action) in view of Steinman et al (WO 93/20185) and Sallusto et al (Journal of Experiemntal Medicine, 1994, vol. 179, pp. 1109-1118) and De La Salle et al ('Fcgr on Human Dendritic Cells' In:Human IgG Receptors, 1996, pp. 39-55, Van de Winkel et al Eds) as applied to claims 1-3, 5, 6, 14, 15, 18-20, 24 and 25 above and in further view of Aruffo et al (US 5,709,859, cited in the previous Office action) and Schlom (In: Molecular Foundations of Oncology, 1991, pp. 95-133).

Claim 8 embodies the method of claim 1 wherein the immunoglobulin heavy chain constant region is an immunoglobulin heavy chain constant region present in the same species as the mammal. Claim 9 embodies the method of claim 8 wherein the immunoglobulin heavy chain constant region is a human immunoglobulin heavy chain constant region. Claim 26 embodies the composition of claim 15 wherein the immunoglobulin heavy chain constant region is a human immunoglobulin heavy chain constant region.

Schlom teaches that HAMA response develop in more than 90% of patients receiving more than three doses of a monoclonal murine Antibody and that it is unrealistic to assume that one or two doses or a given anti-cancer therapeutic would be effective. Schlom concludes that because of the HAM response only the first and perhaps the second administration of the antibody actually reached the tumor site in a therapeutically effective amount. Schlom teaches the use of recombinant chimeric antibodies contain a human Fc region to avoid the HAMA

response (page 98 second column, second full paragraph to page 99, first column, first paragraph).

Aruffo et al teach that fusion proteins comprising extracellular domains of endothelial and granulocyte surface receptors fused to a human IgG constant region are less immunogenic than non human IgG (column 8, lines 54-60).

It would have been prima facie obvious at the time the invention was made to use the human Fc region in the fusion proteins rendered obvious by the combination of Falkenberg et al and Steinman et al and Sallusto et al and de la Salle et al . One of skill in the art would have been motivated to do so by the teachings of Schlam et al regarding the necessity of administering anti-cancer immune agent more than one time to patients having tumors and the necessity of avoid the HAMA response and the teachings of Aruffo et al on the reduction in immunogenicity between fusion proteins comprising Fc from human IgG relative to non human IgG.

Claims 1-3, 5, 6, 7, 14, 15, 18-20, 24 and 25 are rejected under 103(a) as being unpatentable over Falkenberg et al (US 6,406,689, cited in the previous Office action) in view of Steinman et al (WO 93/20185) and Sallusto et al (Journal of Experimental Medicine, 1994, vol. 179, pp. 1109-1118) and De La Salle et al ('Fcgr on Human Dendritic Cells' In:Human IgG Receptors, 1996, pp. 39-55, Van de Winkel et al Eds) as applied to claims 1-3, 5, 6, 14, 15, 18-20, 24 and 25 above and in further view of Blumberg et al (US 6,086,875, cited in the previous Office action).

Claims 1 and 15 recite antigens selected from the group consisting of viruses. Neither Falkenberg et al, Steinman et al, Sallusto et al nor de la Salle et al teach antigens which are viral antigens.

Blumberg et al teach a composition and method for eliciting an immune response in a mammal comprising administration of antigens coupled to molecules that bind to the FcRn. Preferred embodiments of said molecules are non-specific IgG and the Fc fragment of IgG (column 3, lines 26-50). Blumberg et al teach that the antigen is covalently coupled to the FcRn binding partner . Blumberg et al teach antigens which are viral (column 6, lines 20-34). Blumberg et al teach that a variety of administration routes are available depending on the particular conjugates selected, the particular condition being treated and the dosage required for

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therapeutic efficacy (column 9, lines 58-65). Blumberg et al do not teach a fusion protein comprising a viral antigen and the Fc portion of an immunoglobulin.

It would have been *prima facie* obvious to one of skill in the art at the time the invention was made to administer a fusion protein comprising viral antigen fused to the Fc domain of an immunoglobulin in place of a tumor antigen fused to the Fc domain of an immunoglobulin in a method of enhancing the immunogenicity of a viral antigen as an alternative to the method of enhancing the immunogenicity of a tumor antigen rendered obvious by the combination of Falkenberg et al and Steinman et al and Sallusto et al and de la Salle et al. One of skill in the art would have been motivated to do so by the teachings of Blumberg et al on the elicitation of an immune response upon administration of a viral antigen coupled to Fc or to IgG. One of skill in the art would realize that the viral antigen coupled to the Fc or non-specific IgG is being taken up and processed by dendritic cells and that a fusion protein comprising a viral antigen fused to the Fc domain would also be taken up and processed by dendritic cells leading to an enhanced antigen presentation to T-cells.

Claims 1-3, 5, 6, 7, 14, 15, 18-20, 24 and 25 are rejected under 103(a) as being unpatentable over Falkenberg et al (US 6,406,689, cited in the previous Office action) in view of Steinman et al (WO 93/20185) and Sallusto et al (Journal of Experimental Medicine, 1994, vol. 179, pp. 1109-1118) and De La Salle et al ('Fcgr on Human Dendritic Cells' In: Human IgG Receptors, 1996, pp. 39-55, Van de Winkel et al Eds) as applied to claims 1-3, 5, 6, 14, 15, 18-20, 24 and 25 above and in further view of Israeli et al (US 5,538,866, cited in the previous Office action).

Claims 1 and 15 recite antigens selected from the group consisting of PSMA. Falkenberg et al teach antigenic material selected from portions of prostate carcinoma cells (column 20, line 65 to column 21, line 4) but do not specifically identify PSMA as a tumor antigen. Neither Steinman et al, Sallusto et al nor de la Salle et al teach an antigen which is PSMA.

Israeli et al teach PSMA as a protein which is highly expressed in prostate cancer including metastatic prostate cancer (column 3, lines 8-11).

It would have been *prima facie* obvious to use PSMA as a tumor antigen in a fusion protein comprising PSMA fused to the Fc constant region in the method rendered obvious by the combination of Falkenberg et al and Steinman et al and Sallusto et al and de la Salle et al. One

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of skill in the art would have been motivated to do so by the teachings of Israeli et al on the PSMA as a tumor antigen linked to prostate cancer. One of skill in the art would be motivated to enhance the immunogenicity of said antigen in order to elicit an endogenous immune response against cells expressing said antigen.

Claims 1-3, 5, 6, 7, 14, 15, 18-21, 24 and 25 are rejected under 103(a) as being unpatentable over Falkenberg et al (US 6,406,689, cited in the previous Office action) in view of Steinman et al (WO 93/20185) and Sallusto et al (Journal of Experimental Medicine, 1994, vol. 179, pp. 1109-1118) and De La Salle et al ('Fcgr on Human Dendritic Cells' In: Human IgG Receptors, 1996, pp. 39-55, Van de Winkel et al Eds) as applied to claims 1-3, 5, 6, 7, 14, 15, 18-20, 24 and 25 above, and in further view of Krieg et al (US 6,429,199).

Claim 21 embodies the composition of claim 15 wherein the adjuvant comprises an oligonucleotide CpG sequence.

None of the aforestated references teaches the administration of CpG as an adjuvant.

Krieg et al teach methods for activating dendritic cells for use in methods such as cancer therapy comprising the administration of CpG as an adjuvant (column 4, lines 66-67 and abstract).

It would have been prima facie obvious at the time the invention was made to use CpG in place of IL-2 as an adjuvant in the method rendered obvious by the combination of Falkenberg et al and Steinman et al and Sallusto et al and de la Salle et al. One of skill in the art would have been motivated to do so by the teachings of Krieg et al on the activation of dendritic cells in vivo in human subjects.

All other rejections and objections as set forth in the previous Office action are withdrawn in light of applicants amendments and arguments.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

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A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A Canella whose telephone number is (571)272-0828. The examiner can normally be reached on 10 a.m. to 9 p.m. M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on (571)272-0871. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Karen A. Canella, Ph.D.

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04/05/04

Karen A. Canella
KAREN A. CANELLA PH.D
PRIMARY EXAMINER